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Executive Office of Health and Human Services

Clinical Practice Guidelines for the Treatment of Schizophrenia in Adults

Department of Mental Health
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TABLE OF CONTENTS

Introduction

Guideline Recommendations

Appendices

CLINICAL PRACTICE GUIDELINES FOR THE TREATMENT OF SCHIZOPHRENIA IN ADULTS

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MISSION STATEMENT

The intent of these treatment guidelines is to encourage the use of effective treatments, to avoid treatments that are ineffective or unnecessary, and to allow clinical judgment to guide efforts, when there is not sufficient literature. These guidelines define standard practice for the treatment of schizophrenia as supported by published empirical studies. In complicated or atypical cases, clinicians often try less conventional treatments. As the outcome literature is updated, these guidelines will be updated.

The guidelines begin at the point where the clinician has diagnosed schizophrenia according to the criteria for this disorder as defined by the DSM-IV (American Psychiatric Association, 1997), and has evaluated the client for the presence of other medical factors which may affect the diagnosis or treatment of the individual.

The state's Department of Mental Health (DMH) and Division of Medical Assistance (DMA) wish to define standard practice for the following reasons:

- *to ensure that practice patterns conform with empirically supported outcomes literature,*
- *to identify variations in clinical practice,*
- *to guide quality improvement projects,*
- *to structure orientation and training for clinicians,*
- *to provide reference points for utilization review, and*
- *to provide educational reference for individuals with schizophrenia and their families.*

DEVELOPMENT OF THE GUIDELINES

The Clinical Practice Guidelines for the Treatment of Schizophrenia were developed by a Design Committee jointly appointed by DMH and DMA. This committee reviewed existing treatment guidelines that included those by the American Psychiatric Association (APA;1994), the Expert Consensus Guidelines (Frances et al., 1996), the Schizophrenia Patient Outcomes Research Team (PORT: Lehman et al., 1998), the Veterans Health Administration (VAMC;1997), and the Vermont State Mental Health Authority (SMHA,1997). The committee decided to base the guidelines primarily on the PORT Guidelines, and adopted the PORT Guidelines with the following revisions and additions:

- *Committee additions to the PORT recommendations and tables are italicized (words originally italicized in PORT appear as capital letters),*
- *Sections added from other guidelines are bracketed and referenced appropriately,*
- *After PORT Recommendation 30, the committee added Recommendations 31-35. These recommendations include topics and references not included in the PORT,*
- *Appendices I-III present the PORT Tables 1-3,*
- *Appendices IV and V present sample algorithms for Maintenance Psychopharmacology Treatment of Schizophrenia and Treatment Resistant Schizophrenia. (These are offered as examples that may be used in the implementation of relevant recommendations.),*
- *Appendix VI outlines a table to assist in identifying levels of recovery from psychotic disorders,*
- *Appendix VII is the introduction to the original PORT Guidelines.*

This document is intended for the treatment of individuals eighteen years of age or older. While many treatment issues are relevant for younger persons, the assessment and treatment of children and younger adolescents are sufficiently different to warrant separate guidelines, and the interested reader is referred to the American Academy of Child and Adolescent Psychiatry guideline on this topic (1994).

GENERAL CONSIDERATIONS FOR THE TREATMENT OF SCHIZOPHRENIA

[These guidelines address three major areas of consideration in providing care for individuals with serious mental illness: 1.) phases of illness, 2.) components of treatment, and 3.) sites of *treatments.* Only after all three areas are accounted for in the treatment plan will the treatment plan be complete.

- Serious mental illnesses can be long-term illnesses that require an unlimited duration of supports and treatments.
- Serious mental illnesses have the potential to affect all aspects of a person's life and adequate treatment requires attention to any and all of these areas of life.
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- Growing evidence suggests that early interventions may improve the course of the illness.
- Serious mental illnesses may be characterized by relapses and remissions, and adequate care requires a capacity to manage all phases of the illness.
- Recovery is the desirable outcome goal and involves assisting persons to learn how to manage their own illness and treatments. *Recovery is defined as maximizing functioning and well-being and minimizing disability.*
- A comprehensive evaluation is essential and should, at a minimum, include *individual* and family goals, biological issues, functional capacities, substance use, safety issues, stressors, social supports, and general living conditions.
- The *individual* and his/her significant others should be involved in developing the service plan.
- The treatment team may need to provide the impetus for services via assertive outreach and engagement.] [Review Reference: Vermont SMHA, 1997, p. 3.]
- *Service delivery should emphasize the needs of the whole person. Consideration should be given to medical, psychiatric, spiritual, social, family, and vocational issues.*
- *Cultural competent practice needs to incorporate understanding and responsiveness to the beliefs, values, customs, institutions (family, religion, etc.), and ethnic heritage of the person into the treatment planning.*
- *For patients who are not responsive to the clinical recommendations noted herein, sound alternate treatment plans following from sound clinical judgment should be developed.*

THERAPEUTIC ALLIANCE

- [A supportive therapeutic relationship should be established in order for the *individual* to trust the clinician and the team, and thus collaborate with treatment. This relationship will also inform the clinician of early symptom relapse.
- The clinician and/or team should create an atmosphere in which the *individual* can feel free to discuss what he/she experiences as negative in the treatment process so that continued participation in meaningful and effective treatments is enhanced.

- Periodic reassessment of the treatment plan, *including a psychosocial history*, in collaboration with the *individual,* to make modifications in accord with the *individual's* preferences and needs should be practiced.] [Review Reference: Vermont SMHA, 1997, p. 4.]
- *The clinician and/or team should work closely with the individual's family when permission is given.*
- *Deciding about which treatments are pursued is a shared process between the individual seeking services and the clinician. The capacity to engage in treatment planning and decision making is presumed for all individuals seeking services. Clinicians are also obligated to make an assessment of every person's capacity to make decisions. This capacity includes the decision to discontinue treatment and needs to be performed in an initial and ongoing manner. Four generally accepted elements of this capacity are the ability to: 1.) communicate choices, 2.) understand relevant information, 3.) appreciate the situation and its consequences, and 4.) compare risks and benefits of various treatments. Based on this assessment, the clinician is bound by good clinical practice and Massachusetts law, as appropriate. (Review Reference: Appelbaum and Grisso, 1998).*

USING THESE GUIDELINES

[The PORT Treatment Recommendations *and the additional DMH Recommendations* are organized according to categories of treatments, consistent with the framework of the recently completed review of the treatment literature by the PORT-- see the SCHIZOPHRENIA BULLETIN, Vol. 21, No. 4, 1995. The treatment categories are (1) antipsychotic medications; (2) adjunctive pharmacotherapies for anxiety, depression, and aggression/hostility; (3) electroconvulsive therapy; (4) psychological treatments; (5) family treatments; (6) vocational rehabilitation; and (7) assertive community treatment/intensive case management. For each recommendation, a brief rationale and annotations to the to the above referenced issue of SCHIZOPHRENIA BULLETIN are provided. *The DMH recommendations include recently reviewed and updated references.* These earlier literature reviews offer extensive bibliographies.

The level of evidence for each recommendation is also provided. In writing the recommendations, the PORT investigators adopted the criteria on levels of evidence used for the development of the AHCPR (*Agency for Health Care Policy and Research*) Depression Guidelines (U.S. Department of Health and Human Services, 1993) as follows:

Level A: Good research-based evidence, with some expert opinion, to support the recommendation
Level B: Fair research-based evidence, with substantial expert opinion, to support the recommendation
Level C: Recommendation based primarily on expert opinion, with minimal research-based evidence, but significant clinical experience.] [Review reference: Lehman et al., 1998, p.2]

COMMENTS AND FEEDBACK

Any comments or feedback on these guidelines or their implementation should be sent to:

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DISCLAIMERS

PORT Guidelines

The State of Massachusetts is responsible for the content of this document, which was adapted from the Schizophrenia Patient Outcomes Research Team (PORT) Treatment Recommendations *(Schizophrenia Bulletin, 24, 1-11, 1998).* The PORT Treatment Recommendations were developed by Dr. Anthony F. Lehman and colleagues at the Center for Research on Services for Serious Mental Illness (at Johns Hopkins University and the University of Maryland, Baltimore), the University of Maryland Center for Mental Health Services Research, and the Maryland Psychiatric Research Center (at the University of Maryland). Funding for the Schizophrenia PORT project was provided by the Agency for Health Care Policy and Research and the National Institute of Mental Health. This document does not represent the viewpoints of the Agency for Health Care Policy and Research, the National Institute of Mental Health, the University of Maryland, or the Johns Hopkins University.

Department of Mental Health Disclaimer:

These guidelines are meant to provide an overview of uncomplicated treatment of persons with schizophrenia. Care for patients needs to be individualized, and there may be individual circumstances where legitimate and appropriate concerns indicate the needs for interventions that depart from the more common recommendations.

GUIDELINE RECOMMENDATIONS

Pharmacotherapies: Treatment of Acute Symptom Episodes.

Recommendation 1. Antipsychotic medications, *both typicals and atypicals,* other than clozapine, should be used as the first-line treatment to reduce psychotic symptoms for persons experiencing an acute symptom episode of schizophrenia.

RATIONALE. Over 100 randomized double-blind studies consistently support the efficacy of antipsychotic medications relative to placebo in the reduction of the acute positive symptoms (hallucinations, delusions, thought disorganization, bizarre behavior) of schizophrenia. Approximately 50 to 80 percent of persons will improve significantly with this treatment compared with about 5 to 45 percent on placebo. (Review references: Dixon et al., 1995, p. 568; Umbricht and Kane 1995, p. 603; Level of evidence: A)

Recommendation 2. The dosage of antipsychotic medication for an acute symptom episode should be in the range of 300-1,000 chlorpromazine (CPZ) equivalents per day for a minimum of 6 weeks. Reasons for dosages outside this range should be justified. The minimum effective dose should be used. (Cross reference tables of CPZ dose equivalents of various antipsychotic agents are included in tables 1-3 *in Appendices I-III.*) *For all drugs, dosing should be flexible and should be adjusted to maximize efficacy and minimize side effects. Age, gender, physical size, and ethnicity may influence dosing requirements.*

RATIONALE. Randomized clinical trials have consistently found that acute positive symptoms in most persons respond to a daily dose of an antipsychotic medication between 300 and 1,000 CPZ equivalents administered for a minimum of 6 weeks. The risk of suboptimal response increases substantially below this range, and there is little evidence of further benefit above this range. Higher doses also carry an increased burden of side effects. (Review reference: Dixon et al. 1995, p. 569; Level of evidence: A)

Recommendation 3. Persons experiencing their first acute symptom episode should be treated with an antipsychotic medication other than clozapine, but dosages should remain in the lower end of the range mentioned in Recommendation 2 (300-500 mg CPZ equivalents per day).

RATIONALE. Recent studies indicate that persons experiencing their first episode of acute symptoms of schizophrenia respond as well or better to antipsychotic medications in terms of symptom reduction than persons experiencing a recurrent episode. They may also respond to somewhat lower doses. Although "watchful waiting" is an alternative approach raised by concerns about medication side effects, this option is mitigated by concerns that persistent psychosis may complicate the subsequent course of illness. (Review reference: Dixon et al. 1995, p. 574; Level of evidence: B)

Recommendation 4. Massive loading doses of antipsychotic medication, referred to as the practice of "rapid neuroleptization," should not be used.

RATIONALE. Rapid loading doses of antipsychotic medications have shown no general advantage over more moderate dosing approaches (see Recommendation 2). They also carry a significant side-effect burden. Rapid initiation of antipsychotic treatment is important at the outset of an exacerbation, but not a rapid loading dose. (Review reference: Dixon et al. 1995, p. 69, Level of evidence: A)

Recommendation 5. Since studies have found no superior efficacy of any antipsychotic medication over another in the treatment of positive symptoms, except for clozapine in treatment-refractory patients, choice of antipsychotic medication should be made on the basis of patient acceptability, prior individual drug response, individual side-effect profile, and long-term treatment planning and cost. *Generally, conventional antipsychotic agents do not vary significantly in efficacy, but do vary in side effects. The newer atypical agents (Risperidone,*

Olanzapine, Quetiapine) are generally comparable to conventional antipsychotic agents in efficacy for positive symptoms, whereas certain agents in the group may be more effective than conventional agents for the treatment of negative symptoms. Atypical agents may be better tolerated by some patients. Clozapine is more effective for both positive symptoms and negative symptoms than conventional agents, but should not be used first-line.

RATIONALE. As above, studies have found no superior efficacy of any of the antipsychotic medications relative to each other in the treatment of positive symptoms. (Review reference: Dixon et al. 1995, p. 573; *Kane et al., 1988; Marder and Meibach, 1994; Beasley et al., 1996*; Level of evidence: A for equivalent efficacy; C for other factors affecting medication choice)

Recommendation 6. Monitoring of plasma levels of antipsychotic medications should be limited to the following circumstances: (1) when patients fail to respond to what is usually an adequate dose; (2) when it is difficult for the clinician to discriminate drug side effects - particularly akathisia or akinesia - from symptoms of schizophrenia such as agitation or negative symptoms (a high blood level might be associated with increased adverse effects); (3) when antipsychotic drugs are combined with other drugs that may affect their pharmacokinetics; (4) in the very young, the elderly, and the medically compromised in whom the pharmacokinetics may be significantly altered; and (5) when noncompliance is suspected. Plasma levels are most useful when using haloperidol, which has only one active metabolite. *Clozapine plasma levels also may be clinically useful, particularly since high levels resulting from drug interactions can produce serious medical consequences.*

RATIONALE. In general, there is at best a moderate correspondence between plasma drug level and clinical response to antipsychotic medications. Studies suggest an inverted-U or therapeutic window response such that persons with moderate plasma levels of haloperidol show a better clinical response than those with low or high levels. The upper end of this therapeutic window is often defined by side effects. Inadequate clinical response to apparently adequate dosages of antipsychotic medications warrants assessment of plasma levels to rule out unusual or altered drug metabolism or noncompliance. (Review references: Baldessarini et al. 1990; Kane and Marder 1993; Level of evidence: B)

Recommendation 7. Prophylactic use of anti-Parkinson agents to reduce the incidence of extrapyramidal side effects (EPS) should be determined on a case-by-case basis, taking into account patient and physician preferences, prior individual history of EPS, and other risk factors for both EPS and anticholinergic side effects. The effectiveness of and continued need for anti-Parkinson agents should be assessed in an ongoing fashion. *Newer atypical antipsychotic agents are unlikely to require prophylactic treatment with anti-Parkinson agents.*

RATIONALE. Although the data are clear that anti-Parkinson agents are effective in reducing or eliminating the EPS of antipsychotic medications, experts disagree about the advisability of using these agents prophylactically. The controversy arises in weighing the risks of EPS against those of the side effects of anti-Parkinson agents. Prophylaxis may be especially important among persons with a prior history of noncompliance or drug discontinuation related to EPS and among persons for whom even mild EPS may lead to drug aversion (e.g., among patients with paranoia or somatic delusions). Avoidance of anticholinergic effects may be especially important in the elderly and in individuals with a history of anticholinergic crises. *Anticholinergic agents at typical clinical doses may produce substantial memory impairment.* (Review references: Rifkin and Siris 1987; Davis et al. 1989; Level of evidence: B)

Pharmacotherapies: Maintenance Pharmacotherapy. (*See Appendix IV.)*

Recommendation 8. Persons who experience acute symptom relief with an antipsychotic medication should continue to receive this medication for at least 1 year subsequent to symptom stabilization to reduce the risk of relapse or worsening of positive symptoms.

RATIONALE. More than 30 clinical trials have confirmed that maintenance therapy with an antipsychotic medication after an initial positive response during an acute symptom episode significantly reduces the risk of symptom relapse during the first year after the acute symptom episode. On average, persons on maintenance therapy experienced symptom relapse over a follow-up year at a rate of about 20 to 25 percent compared with about 55 percent for those on placebo. The value of maintenance therapy beyond the first year has not been studied extensively. (Review reference: Dixon et al. 1995, pp. 569-570; Level of evidence: A)

Recommendation 9. The maintenance dosage should be in the range of 300 to 600 CPZ equivalents (oral or depot) per day. If the initial dosage to relieve an acute symptom episode exceeds this range, efforts should be made to reduce the dosage gradually to this range, such as a 10 percent reduction in dosage every 6 weeks, until either early signs of relapse begin to emerge or until the lower level of this recommended range is achieved (see Recommendation 2). The new maintenance dosage should be at the last level at which symptoms were well controlled. Dosages in excess of 600 CPZ equivalents per day should be avoided unless symptom control and patient comfort are clearly superior at these higher dosages. The lowest effective dose should be used, *which may fall below 300 mg. Chlorpromazine-equivalents per day for some patients, and should be adjusted for age, gender, physical size, and ethnicity.*

RATIONALE. Maintenance therapy trials have found that maintenance doses below 300 mg CPZ equivalents per day carry an increased risk of relapse, although a substantial proportion of persons (up to 50%) can be maintained successfully at these lower doses, warranting a gradual and carefully monitored effort to reduce dosage over time. There is no evidence that maintenance doses above 600 mg CPZ equivalents per day confer any additional advantage in general. (Review reference: Dixon et al. 1995, pp. 570-572; Level of evidence: A) (*See Appendices I-IV.*)

Recommendation 10. Reassessment of the dosage level or the need for maintenance antipsychotic therapy should be ongoing. Patients who have had only one episode of positive symptoms before initiation of antipsychotic therapy and who have experienced NO positive symptoms during the year of maintenance therapy should be given *consideration for* a trial period off medication, *following a gradual tapering,* and assuming they are aware of the potential risk of relapse and agree to this plan. For patients with more than one prior episode who have experienced good symptom control on the medication during the preceding year, maintenance therapy should be continued unless unacceptable side effects or some other contraindications to antipsychotic treatment have developed. If the maintenance dosage has been high (>600 CPZ equivalents) during the past year, attempts to lower the dosage as described in Recommendation 9 should be considered. Reasons for not attempting to lower dosage should be clearly indicated, such as patient preference in the face of concerns about symptom relapse or life stressors that militate against attempts to lower medications.

RATIONALE. Clinical trials of maintenance antipsychotic therapy have generally not followed patients in maintenance therapy beyond 1 year, and thus evidence regarding long-term maintenance is lacking (see also rationale for Recommendation 8). (Review references: Kissling 1992; Dixon et al. 1995, pp. 570-571; Level of evidence: C)

Recommendation 11. Targeted, intermittent dosage maintenance strategies should not be used routinely in lieu of continuous dosage regimens because of the increased risk of symptom worsening or relapse. These strategies may be considered for patients who refuse maintenance

or for whom some other contraindication to maintenance therapy exists, such as side-effect sensitivity.

RATIONALE. The relatively few studies of targeted, intermittent dose strategies suggest that the relapse rate is higher than for continuous maintenance therapy. Therefore, this approach is recommended only for the circumstances identified above. (Review reference: Dixon et al. 1995, pp. 570-571; Level of evidence: B)

Recommendation 12. Depot antipsychotic maintenance therapy should be strongly considered for persons who have difficulty complying with oral medication or who prefer the depot regimen. Depot therapy may be used as a first-option maintenance strategy.

RATIONALE. Controlled trials have produced inconsistent results with regard to whether depot medication reduces the risk of relapse in comparison with oral medication. However, the design of these studies, which by definition include persons willing to accept medication in a clinical trial, may bias against any advantage of depot medication. Further, the duration of these studies has been inadequate to demonstrate a strong advantage for depot medication. In persons for whom compliance is a problem, depot medication offers clear advantages if it is accepted by the patient. If acceptable to the patient, depot medication is just as appropriate as oral medication as the first-line maintenance therapy strategy. (Review reference: Dixon et al. 1995, p. 573; Level of evidence: B) *(See Appendices II and III.)*

Pharmacotherapies: New Antipsychotic Medications.[1]

Recommendation 13. A trial of clozapine should be offered to patients with schizophrenia or schizoaffective disorder whose positive symptoms do not robustly respond to adequate trials of two different classes of antipsychotic medications. Exceptions include patients who cannot receive clozapine due to a history of blood dyscrasia or cardiac arrhythmia. Lack of response to previous antipsychotic trials is defined by persistent symptoms after two 6-week trials of up to 1,000 CPZ equivalents of antipsychotic agents from two different chemical classes (e.g., phenothiazines and butyrophenones). *Prior to proceeding to clozapine, one of these trials should include at least one atypical agent.* An adequate clozapine trial should last 3 months at a dosage from 300 to 800 mg per day. *The maximum dose approved by the FDA is 900 mg. a day, and may be required for efficacy in some patients.* Dosages should reflect the lowest possible effective dose. If patients do not respond, a blood level should be obtained and dosages slowly increased to 800 mg to the extent that side effects are tolerated. If effective, clozapine should be continued as maintenance therapy.

RATIONALE. Controlled clinical trials have found that clozapine produces significant clinical improvement in at least 30 percent of patients who fail to achieve an adequate response to or cannot tolerate conventional antipsychotic medications. It should be considered only after other antipsychotic medications prove inadequate because of its low but significant risk of agranulocytosis, complexity of management (*initially weekly, then bi-weekly* white cell count reports), and cost. *Clozapine is often cost-effective by reducing use of hospitalization.* The level of evidence for the differential effectiveness of clozapine among outpatients is limited by the low number of studies of outpatients. (Review references: Buchanan 1995, pp. 580-584;

[1] As of the writing of these recommendations *PORT* September 1996, additional antipsychotic agents were expected to reach the market within the next 1 to 2 years. These agents include olanzapine, quetiapine, sertindole, *rispersidone*, and ziprasidone. No recommendations specific to these newer compounds are included because the level of data on them is more limited than for clozapine and risperidone. Until proven otherwise, the use of these newer compounds, when marketed, should follow the recommendations for antipsychotic agents other than clozapine.

Meltzer et al., 1993; Rosenheck et al., 1997; Level of evidence: A for inpatients; B for outpatients;)

Recommendation 14. A trial of clozapine should be offered to patients with schizophrenia or schizoaffective disorder who have repeatedly displayed violent behavior and persistent psychotic symptoms that have not been responsive to trials of at least two different types of antipsychotic medications (as defined in Recommendation 13).

RATIONALE. Randomized clinical trials, as well as nonrandomized studies, suggest that clozapine significantly reduces hostility among treatment-refractory patients. It should only be considered after other antipsychotic medications prove inadequate. (Review reference: Buchanan 1995, p. 582; Level of evidence: B)

Recommendation 15. A trial of clozapine should be *considered for* patients who require antipsychotic therapy, but who experience intolerable side effects to other antipsychotic agents, including severe or very distressing tardive dyskinesia, persistent dystonia, and neuroleptic malignant syndrome. *A trial of an atypical agent other than clozapine should be conducted in patients who do not tolerate neuroleptic-induced EPS prior to proceeding to clozapine. Preliminary evidence suggests that other atypicals may also reduce the risk of tardive dyskinesia.*

RATIONALE. A limited body of evidence suggests that clozapine causes substantially less tardive dyskinesia than antipsychotic medications, although there are reports of cases in which tardive dyskinesia has worsened on clozapine. For the patient with severe tardive dyskinesia for whom ongoing treatment with another antipsychotic agent poses a substantial risk of continuation or further progression of the movement disorder, but for whom antipsychotic therapy is essential to prevent serious relapse, a trial with clozapine is indicated. (Review reference: Buchanan 1995, p. 587; Level of evidence: B)

Recommendation 16. Persons who achieve an adequate reduction in positive symptoms on conventional antipsychotic medications, but who have significant EPS that do not respond adequately to anti-Parkinson agents, should be offered a trial of an *atypical agent.* Per Recommendation 1, atypical agents (e.g.: risperidone, olanzapine, quetipane and ziprasidone) can be used as first-line medications.

RATIONALE. In clinical trials, risperidone *(and other newer atypical agents)* have been found to be at least as effective as other antipsychotic medications in reducing the positive symptoms of schizophrenia. Risperidone's major potential advantage over conventional antipsychotic medications is that it produces fewer EPS at the lower end of its effective dose range (4-10 mg per day). *Available evidence also indicates that the newer atypical agents also produce fewer EPS.* Therefore, for patients on the older antipsychotic agents and in whom EPS is a significant problem, risperidone *and other atypical agents* offer an alternative. (Review reference: Umbricht and Kane 1995, pp. 602-604; Level of evidence: B)

Recommendation 16A. *Persons treated with conventional antipsychotic agents who exhibit persistent negative symptoms should be offered a trial of an atypical antipsychotic agent. A trial of an atypical antipsychotic agent should last from 6 to 12 weeks.*

RATIONALE. Parkinsonian side effects of conventional antipsychotic agents and depression may mimic primary negative symptoms. If present, these causes of "secondary negative symptoms" should be identified and treated. Risperidone and olanzapine have been shown to be more effective than haloperidol for the treatment of negative symptoms; superior efficacy of other atypical agents for negative symptoms has not yet been fully established. (Review references: Carpenter, 1996; Marder and Meibach, 1994; Beasley et al., 1996)

Pharmacotherapies: Adjunctive Pharmacotherapies.

Recommendation 17. Persons who experience persistent and clinically significant, associated symptoms of anxiety, depression, or hostility, despite an adequate reduction in positive symptoms with antipsychotic therapy, should receive a trial of adjunctive pharmacotherapy. A trial of benzodiazepine, (*Buspirone*) or propranolol is merited for persistent anxiety. *Benzodiazepines should be used cautiously in the treatment of persons with co-occurring serious mental illness and substance abuse.* An antidepressant trial should be considered for persistent depression. Adjunctive therapy with lithium, a benzodiazepine, or carbamazepine should be considered for persistent hostility or manic-like symptoms. The reasons for the absence of such trials for appropriate patients should be documented. *When adding adjunctive medication, side effects should be closely monitored and the adjunctive medication should be tapered and discontinued if no clear clinical benefit is apparent after a reasonable trial.* Certain adjunctive medications should be avoided in patients currently receiving clozapine to avoid synergistic side effects; for example, respiratory depression with (HIGH-DOSE) benzodiazepines and bone marrow suppression with carbamazepine.

RATIONALE. Anxiety and tension may respond to treatment with adjunctive benzodiazepines, although a few studies reported a waning effect of these agents, perhaps due to tolerance, after a few weeks of treatment. Disruptive, dangerous, or assaultive behavior may be modified by the addition of benzodiazepines or carbamazepine to an antipsychotic regimen. *Addition of carbamazepine may lower blood levels of haloperidol and possibly other antipsychotic agents, resulting in worsening of psychosis.* Evidence of the usefulness of benzodiazepines for this indication comes from open or retrospective studies, and no double-blind studies have thus far addressed this. Similarly, these behaviors are cited as potentially responsive to adjunctive carbamazepine, although most evidence is from open studies, with only one positive double-blind study. Excitement and irritability (often classified as "affective symptoms") seem to benefit from adjunctive lithium treatment, with a small amount of evidence that benzodiazepines and carbamazepine also might be useful. Antidepressants seem to benefit patients who have episodic signs and symptoms of depressive illness in addition to schizophrenia, if they are administered in phases of illness other than the active, psychotic exacerbation phase. Antidepressants can be efficacious without exacerbating psychotic symptoms when used adjunctively with antipsychotics. Most studies of adjunctive treatments for schizophrenia were done with patients who had chronic schizophrenia and who were often designated as treatment refractory. Little is known about the efficacy of adjunctive agents for first-episode schizophrenia, for patients experiencing acute episodes of psychosis, or for stable patients receiving maintenance antipsychotic therapy. Little is known about the long-term effectiveness of adjunctive agents. (Review references: Johns and Thompson 1995, pp. 612-613; *Goff and Baldessarini, 1993;* Level of evidence: B)

Recommendation 18. Persons who experience persistent and clinically significant positive symptoms despite adequate antipsychotic therapy, including trials with the newer antipsychotics (clozapine, risperidone *or other atypical agents*), should receive a trial of adjunctive pharmacotherapy as described in Recommendation 17.

RATIONALE. No adjunctive agent has demonstrated clear and consistent benefit in a majority of persons with schizophrenia. However, the most promising agents are the benzodiazepines (which may be useful in as many as 50% of patients with schizophrenia), lithium, and carbamazepine (which may be of mild or modest value to treatment-nonresponsive patients). Very little evidence supports a role for adjunctive propranolol. Valproate, calcium channel blockers, antidepressants, clonidine, and dopaminergic agents have no demonstrated use in terms of global improvement, although they may be useful for individual symptom complexes. Positive symptoms may improve when benzodiazepines, carbamazepine, lithium, or propranolol

are added to antipsychotics. *Addition of carbamazepine may lower blood levels of haloperidol and possibly other antipsychotic agents, resulting in worsening of psychosis.* Adjunctive benzodiazepines produced significant improvements of positive symptoms in about half the double-blind studies that addressed this question. Adjunctive carbamazepine produced significant improvement in only a fraction of double-blind studies. Adjunctive lithium seems to alleviate, to some degree, positive symptoms in a subgroup of patients. Finally, adjunctive propranolol produces only slim evidence of a therapeutic effect on positive symptoms in a minority of double-blind studies. (Review reference: Johns and Thompson 1995, pp. 611-612; Level of evidence: C) *The evidence most strongly supports a trial of clozapine in treatment-resistant patients rather than addition of adjunctive medication to other antipsychotic agents. Data are not available from controlled studies to guide the use of adjunctive medications with clozapine.*

Electroconvulsive Therapy (ECT)

Recommendation 19. Patients who have not responded to recommended antipsychotic therapy should be considered for a trial of ECT alone or in combination with an antipsychotic if (a) the person has been ill for less than 1 year or, if ill for more than 1 year, is in the early phase of an acute exacerbation or (b) affective or catatonic symptoms are predominant.

RATIONALE. There are scientifically sound studies that show that ECT reduces acute symptoms in schizophrenia. Some authors dispute this finding, however, with several pointing to the problem of affective symptoms in schizophrenia and the diagnostic confounding of schizophrenia with affective disorders. The majority of authors indicate that a secondary role is most appropriate, and there is a general consensus that the effects of ECT on schizophrenia are short lived. A few studies with minimal data show continued improvement at follow-up of several years when ECT is followed by maintenance antipsychotic therapy. Catatonic schizophrenia and schizoaffective disorder seem to be most responsive to ECT, and in general the affective symptoms respond selectively to it. (Review reference: Johns and Thompson 1995, pp. 610-611; Level of evidence: B)

Recommendation 20. The dosage of ECT (i.e., number of treatments) used to treat patients with schizophrenia should be comparable to that used for patients with affective disorders (about 12 treatments).

RATIONALE. Three controlled studies found definite improvement after 12 or fewer treatments, and another study indicates that the average number of treatments needed for improvement is 13.6. (Review reference: Johns and Thompson 1995, pp. 610-611; Level of evidence: B)

Recommendation 21. Regressive forms of ECT are NOT recommended for persons with schizophrenia.

RATIONALE. Most reviewers indicate that selected patients with severe and chronic schizophrenia may benefit from modified ECT, but others indicate that the procedure is "drastic," "experimental," and "controversial." (Review reference: Johns and Thompson 1995, pp. 610-611; Level of evidence: C)

Psychological Treatments.

Recommendation 22. Individual and group psychotherapies adhering to a psychodynamic model (defined as therapies that use interpretation of unconscious material and

focus on transference and regression) should NOT be used in the treatment of persons with schizophrenia.

The Design Committee partially disagreed with this PORT recommendation, and added the following statement:

People who have psychotic symptoms still have an active psychological life; therefore supportive psychotherapy techniques may be useful in some of these cases.

RATIONALE. The scientific data on this issue are quite limited. However, there is no evidence in support of the superiority of psychoanalytic therapy to other forms of therapy, and there is a consensus that psychotherapy that promotes regression and psychotic transference can be harmful to persons with schizophrenia. This risk, combined with the high cost and lack of evidence of any benefit, argues strongly against the use of psychoanalytic therapy *(regressive/abreactive psychotherapy),* even in combination with effective pharmacotherapy. (Review reference: Scott and Dixon 1995*b*, p. 623; Level of evidence: C)

Recommendation 23. Individual and group therapies employing well-specified combinations of support, education, and behavioral and cognitive skills training approaches designed to address *the illness, its effects, and* the specific deficits of persons with schizophrenia should be offered over time to improve functioning and enhance other targeted problems, such as medication noncompliance.

RATIONALE. Although the scientific data for this recommendation are limited and flawed, controlled studies have found some additional benefit when a supportive form of psychotherapy is added to pharmacotherapy for persons with schizophrenia. The most effective forms and doses of these therapies and their modes of action remain unknown. (Review reference: Scott and Dixon 1995*b*, pp. 623-627; Level of evidence: B); *Wallace, 1998*

Family Treatments.

Recommendation 24. *When not contraindicated,* persons who have ongoing contact with their families should be offered a family psychosocial treatment. *Such approaches provide a combination of education about the illness, family support, crisis treatment, multiple family therapy treatment, and problem-solving skills. These services should also be offered to non-family caregivers. Persons with schizophrenia often have other people in their lives who are essential to their well-being and the management of symptoms. These individuals may be family, but may include significant others. Services should be offered in an ongoing way and are particularly important early in treatment or in a person's psychiatric hospitalization.*

RATIONALE. Randomized clinical trials have repeatedly demonstrated that family treatments that provide some combination of illness education, support, problem-solving training, and crisis treatment, in combination with appropriate pharmacotherapy, reduce 1-year relapse rates from a 40 to 53 percent range to a 2 to 23 percent range. (Review references: Dixon and Lehman 1995, p. 639; *McFarlane et al., 1995,* Level of evidence: A*.)*

Recommendation 25. Family treatments should not be restricted to patients whose families are identified as having high levels of "expressed emotion" (criticism, hostility, over-involvement).

RATIONALE. Although the earlier controlled trials of family psychoeducation programs focused on the variable of family expressed emotion as a mediator of the impact of this treatment on outcomes, more recent studies have found that these treatments offer substantial benefit to patients and families regardless of the level of expressed emotion. (Review reference: Dixon and Lehman 1995, p. 639; Level of evidence: B)

Recommendation 26. Family therapies based on the premise that family dysfunction is the etiology of the patient's schizophrenic disorder should NOT be used.

RATIONALE. Research has failed to substantiate hypothesized causal links between family dysfunction and the etiology of schizophrenia. Therefore, therapies specifically designed from this premise are not empirically founded. Although there has been little or no randomized, controlled research on the impact of family therapies arising from this orientation, experts in the field have expressed strong caution against the use of these techniques. The presumption that family interaction causes schizophrenia, especially as an alternative to biological risk factors, has led to serious disruption in clinician/family trust without any evidence of therapeutic effectiveness. The repudiation of the theoretical premise of these therapies, the lack of empirical studies, and the strong clinical opinion raising concerns about the potential harm caused by these approaches lead to this recommendation. (Review reference: Dixon and Lehman 1995, p. 631; Level of evidence: C)

[**Recommendation 26A.** Self-help groups, such as the Alliance for the Mentally Ill, should be suggested to families.] *Such groups as peer support and peer dual recovery support groups can be a source of support and education for families, and help decrease stigma associated with mental illness.* [Review reference: APA Guidelines, p. 32.]

Vocational Rehabilitation.

Recommendation 27. Persons with schizophrenia who have ANY of the following characteristics should be offered vocational services. The person (a) identifies competitive employment as a personal goal, (b) has a history of prior competitive employment, (c) has a minimal history of psychiatric hospitalization, and (d) is judged on the basis of formal vocational assessment to have good work skills. *However, recent studies suggest that individuals, regardless of previous work history or level of symptomatology, are capable of competitive employment. Providers should assume that employment opportunities exist. Opportunities for vocational rehabilitation and employment are essential in recovery from schizophrenia. Assessment regarding a person's willingness to participate in vocational programming should be guided by clinical judgment, in addition to the above criteria.* RATIONALE. Controlled studies of vocational rehabilitation treatments for persons with schizophrenia have not shown consistent or significant impacts on outcomes other than those directly related to involvement in the rehabilitation program (e.g., increased involvement in sheltered work). However, these studies have been flawed by the failure to control for individual characteristics that may alter a person's vocational potential. They have identified subgroups of recipients post hoc who benefited from the treatments. The above characteristics have been found to be predictive of better vocational outcomes in persons with schizophrenia, and therefore persons with these characteristics should be offered such services. (Review reference: Lehman 1995, pp. 647-63; *Bond et al., 1996;* Level of evidence: C) *See Appendix VI.*

Recommendation 27A. *Persons with schizophrenia who have any of the following characteristics should be offered Rehabilitation Services including but not limited to Occupational Therapy and Vocational Rehabilitation. The person demonstrates functional deficits that interfere with their goals to participate in and accomplish their daily life responsibilities, life roles, and interests. Such areas include 1) Activities of Daily Living: grooming, dressing, feeding, medication routine, health maintenance, socialization, functional communication, functional mobility, emergency response, 2) Work and Productive Activities: Home management, care of others, educational opportunities, vocational activities, and 3) Leisure Activities: leisure expression, leisure performance. Rehabilitative Services, such as*

Occupational Therapy, provide functional capacity evaluations and treatment in the following areas; 1) Performance Area 2) Performance Components and 3) Performance Contexts.

RATIONALE. One's ability to function successfully is a dovetailing of the functional skills of the individual and the functional demands of the environment. If an individual's ability does not meet the demands of the environment, the individual will fail. Occupational Therapy assesses the individual and environment, to establish the skills needed by the individual as well as the adaptations required of the environment to maximize the individual's functioning. Occupational Therapy provides treatment in the following categories. Performance Area: selfcare, work and leisure, Performance Components: the cognitive and physical ability to engage in the Performance Area; such as strength, fine motor, problem solving, new learning skills, and Performance Contexts: physical, social, and cultural factors that may effect the individual's ability to perform a task. (Review reference: AOTA 1999).

Recommendation 28. The range of vocational *and rehabilitation* services available in a service system for persons with schizophrenia living in the community who meet the criteria defined in Recommendation 27 should include (a) prevocational training, (b) transitional employment, (c) supported employment, and (d) vocational counseling and education services (job clubs, rehabilitation counseling, post-employment services).

RATIONALE. Recent controlled studies have reported significantly improved vocational outcomes for the supported employment model, which emphasizes rapid placement in a real job setting and strong support from a job coach or other employment specialist to adapt to and sustain the job. Therefore, unless ongoing research fails to substantiate these early findings, supported employment should definitely be available to persons meeting the aforementioned criteria. Scientific data supporting the effectiveness of the other forms of vocational services mentioned above are lacking, but some persons who are good candidates for supported employment may benefit from the addition of these services as well, so they are mentioned in the recommendation. (Review reference: Lehman 1995, pp. 647-653; Level of evidence: B)

Service Systems.

Recommendation 29. Systems of care serving persons with schizophrenia who are high service users should include assertive case management (ACM), *intensive case management (ICM), and/or* assertive community treatment (ACT) programs.

RATIONALE. Persons with disabling schizophrenia who are at high risk for discontinuation of treatment or for repeated crises require an array of clinical, rehabilitation, and social services to address their needs. Coordination, integration, and continuity of services among providers over time can be substantially enhanced through ACM and ACT. Randomized trials have demonstrated consistently the effectiveness of these programs in reducing inpatient use among such high-risk patients. Several studies also support improvements in clinical and social outcomes. These studies suggest that ACT, ICM, and ACM are superior to conventional case management for high-risk cases. (Review reference: Scott and Dixon 1995*a*, pp. 659-664; Level of evidence: A)

Recommendation 30. Assertive community treatment programs *(ACM, ICM, or ACT)* should be targeted to individuals at high risk for repeated rehospitalizations or who have been difficult to retain in active treatment with more traditional types of services *or who are dangerous.*

RATIONALE. The original ACT studies reporting efficacy for these approaches targeted these high-risk persons. The efficacy of *ACM, ICM, or ACT* with lower risk patient groups has not been established. The high cost of ACT therefore warrants careful targeting for cost-effectiveness. (Review reference: Scott and Dixon 1995*a*, pp. 659-664; Level of evidence: B)

DEPARTMENT OF MENTAL HEALTH
ADDITIONAL RECOMMENDATIONS

Recommendation 31. *The risk of harm to self or others requires initial and ongoing assessment and should include family, friends, etc., as well as the context when the assessment is made. Appropriate precautions should be taken whenever there are concerns about the safety of the individual or others.*

RATIONALE. Persons in a psychotic state may have high anxiety, faulty reality testing, poor judgment, or diminished impulse control. They may be at risk of harming themselves or others. The evaluation of all individuals with schizophrenia should therefore include a written assessment of past and present suicidal/homicidal thoughts, plans, and acts. It should take into account recent current stress, severity of current symptoms, delusions (especially of influence, persecution and control), substance abuse (especially alcohol) or withdrawal, EPS, and cessation of recent psychotropic medication. If and when the evaluator concludes that imminent harm is likely, there exists an obligation to protect the safety of the individual and of others. If voluntary treatment in a safe setting is refused, involuntary treatment in a safe setting is indicated. (Review references: Appelbaum, 1994; Monahan, 1992; Mulvey, 1994.)

Recommendation 32. *Individuals with schizophrenia should be offered a wide range of services in least restrictive care settings appropriate to their treatment goals and needs. To prevent treatment plan fragmentation, a single clinician should assume responsibility for the coordination and integration of services. This clinician should work with the individual with schizophrenia (and family and significant others, if indicated) to develop a comprehensive written treatment plan that reflects the status of current clinical needs and monitors for the adverse effects of treatment. Continuity of inpatient and outpatient treatment, communication with and education of the family, and actions to take in case of emergency should be essential plan elements. Following implementation, this plan should be revised regularly and be distributed to the individual with schizophrenia and to treating clinicians. To facilitate communication, medical records of multiple providers should be easily and readily shared.*

RATIONALE. Having an identified clinician providing coordination and integration of services leads to constancy and organization of treatment over time. This communication facilitates the transition from inpatient to community treatment settings. When clinicians, residential workers, vocational counselors and family are split or work at cross-purposes, the individual often regresses to a more disorganized and less adaptive level of functioning.

Recommendation 33. *Integrated psychosocial rehabilitation services should be made available to individuals with schizophrenia, where feasible.*

RATIONALE. The recognition that many individuals with schizophrenia need a place in the community that assists them in their efforts to reintegrate into society has led to the development of several psychosocial rehabilitation models. These programs share basic principles that underlie psychiatric rehabilitation, and include: the importance of individual's choice and participation in the development of the individual's rehabilitation, the central role of the concept of recovery, an emphasis on strengths and wellness, skills training, and the importance of work in recovery. Activities focus on vocational, recreational, social, and residential functions. Examples of integrated programs include Fountain House and Fairweather programs which have been replicated nationally, and Fountain House programs now exist internationally. The research data on integrated models is limited, but growing. They suggest that these models lower rehospitalization, succeed in helping individuals to find jobs, and increase social skills.

[**Recommendation 23A.** Psychoeducational treatments should be available to individuals with schizophrenia. The specific focus of this education should include: (a) health education (understanding illness and treatment, alcohol/drug abuse and/or dependence, sexually transmitted diseases, *family planning*, smoking cessation, weight management and nutrition, *physical exercise*, (b) independent living skills, (c) social skills training, and (d) information regarding self-help groups for persons with mental illness *and (e) functional compensation skills*. [VAMC; APA, pgs. 30-32]; *Sousa, 1998, in press; Goisman et al., 1991* .

Information regarding schizophrenia and its treatment should be offered as part of an ongoing educational process, in a language that individuals can understand, and should be based on current research in the field. The educational materials used should be sensitive to the cognitive and specific background of the individual, and be tailored to that individual's learning needs. One method which can be used to increase a person's participation in treatment is the Levels of Recovery from Psychotic Disorders Chart. (See Appendix VI.) This chart serves as a guide for persons to better understand their progress or lack of progress with specific treatments. It can be used over time to prompt the person, treatment team, and family to consider other treatment alternatives and options that may maximize progress towards recovery.]

Recommendation 34. *Schizophrenia and substance dependence (co-occurring disorders) are examples of primary mental, psychiatric or behavioral illness which can utilize a disease and recovery model for conceptualizing assessment and treatment. The recommended treatment approach for co-occurring disorders is integrated dual primary treatment, in which each individual has a primary treatment relationship that coordinates ongoing treatments for each disorder. Each disorder receives specific and appropriately intensive primary treatment which takes into account the complications resulting from the co-occurring disorders. Ideally, each individual can receive treatment for both disorders in the setting or service system in which s/he receives treatment for the more serious disorder(s). Recommended treatments for co-occurring disorders should be individualized, and matched according to specific diagnosis of each disorder, phase of treatment, and recovery, and for the acuity, severity, disability, and motivation for treatment of each disorder at any point in time.*

RATIONALE. Among individuals with serious mental illness, studies have indicated a rate of substance abuse between 32 and 85 per cent and substance dependence of between 15 and 40 per cent. ECA studies indicate a markedly increased prevalence of severe psychiatric disorders among individuals with substance dependence diagnoses. The presence of large numbers of individuals with co-occurring disorders has created significant difficulties for both the addiction and mental health system. Individuals with co-occurring disorders experience worse outcomes in many areas: psychiatric rehospitalization, compliance, homelessness, involvement with the corrections system, medical conditions, and accidental death rate. Recent studies of integrated treatment programs suggest that individuals in such programs achieve remission or recovery from substance abuse at a more rapid rate than conventional programs and experience improvements in other areas such as psychiatric rehospitalization and residential stability. (Review references: Drake et al., 1996; Minkoff, 1991; Regier et al., 1990)

Recommendation 35. [The housing needs of individuals with schizophrenia should be carefully assessed, and a wide range of housing options should be available.

Assessment of Housing Needs.] *A person's choice regarding housing should be respected. If an assessment determines that a person's ability to make this choice is compromised, housing choices must be made in consideration of his or her overall needs as well as preferences.*

[Housing Options. Housing choices should cover a spectrum of needs for an individual including the amount of supervision needed, types of problems, diagnostic needs, necessary medical support, the person's strengths, *and environmental adaptation needs*.

RATIONALE. Assessment of Housing Needs. Persons should reside in the least restrictive setting that is likely to prove safe and effective, and which permits the highest level of functioning. Supportive housing is a psychosocial program widely used for persons who do not live with their families, and who would benefit from some supervision in their living arrangements. Decisions for housing choices may be based on the following considerations: (1) individual preference, (2) family preference, (3) protection of the person from harm to self or others *or environmental safety hazards*, (4) the person's need for external structure and support, (5) the person's ability to cooperate with treatment *and home management skills*, (6) the person's need for a particular treatment or a particular intensity of treatment that may be available only in certain settings, (7) the person's need for a specific treatment for a comorbid general medical or psychiatric condition, and (8) the availability of psychosocial supports *and rehabilitation efforts* to facilitate the person's receipt of treatment and to provide critical information to the clinician or caregiver about clinical status and response to treatments. (Reference Review: APA Guidelines, p. 34)

RATIONALE. Housing Options. Some individuals, because of their disability, may require supervised housing for the duration of the illness. Based on the individual's assessment, housing choices should include: (1) transitional halfway houses or residential facilities providing room and board and promoting socialization, until suitable housing is available; (2) long-term group residences or facilities in which on-site staff are present for chronically functionally disabled individuals, (3) cooperative apartments in which no on-site staff are present, but where there are regular visits by staff for oversight; (4) intensive care or crisis community residences which are used to help prevent hospitalization or shorten the length of hospitalization. Usually there are on-site personnel present; (5) foster or family care in which persons may be placed in private homes; (6) board-and-care homes or rooming houses; (7) nursing homes, which may be suitable for some geriatric or medically disabled chronic persons, *and (8) independent living, including parents and pregnant women.*] [Review ref.: APA, p. 34]

Appendix I

Table 1. Chlorpromazine (CPZ) equivalencies and PORT recommended dosing of antipsychotic medications. See Recommendation 2.

Table 1. Chlorpromazine (CPZ) equivalencies and PORT recommended dosing of antipsychotic medications

			PORT recommended total daily dose range (mg/day)	
Medication	**CPZ equivalence[1]**	**CPZ-equivalence multiplier[2]**	**Acute therapy**	**Maintenance therapy**
Chlorpromazine	100	1	300-1000	300-600
Trifluprom azine	25	4	75-250	75-150
Mesoridazine	50	2	150-400[3]	150-300
Thioridazine	100	1	300-800[3]	300-600
Acetophenazine	20	5	60-200	60-120
Fluphenazine HCI	2	50	6-20	6-12
Perphenazine	10	10	30-100	30-60
Prochlorperzine	15	6	50-150	50-100
Trifluoperazine	5	20	15-50	15-30
Chlorprothixene	100	1	300-1000	300-600
Thiothixene	5	20	15-50	15-30
Haloperidol	2	50	6-20	6-12
Loxapine	10	10	30-100	30-60
Molindone	10	10	30-100	30-60
Clozapine	50	2	200-600	200-800
Risperidone	1	100	4-10	4-10
Olanzapine	3	33	10-20	10-20
Quetiapine	50	2	250-750	250-750
Ziprasidone	*20*	*5*	*80-160*	*80-160*

Note.-PORT = Patient Outcomes Research Team. HCI = hydrochloride. Adapted from Zito 1994 and Kane 1966.

[1]Approximate dose equivalent to 100 mg of chlorpromazine (relative potency); may not be the same at lower versus higher doses.
[2]This number multiplied by the dose of antipsychotic medication results in the chlorpromazine-equivalent dose.
[3]To avoid the risk of retinopathy, doses of 400 mg (mesoridazine) and 800 mg (thioridazine) should not be exceeded.

Appendix II

Table 2. Chlorpromazine (CPZ) equivalencies and dosing of fluphenazine decanoate. See Recommendation 2.

Table 2. Chlorpromazine (CPZ) equivalencies and dosing of fluphenazine decanoate

Decanoate dosing schedule											
Q every week			**Q every 2 weeks**			**Q every 3 weeks**			**Q every 4 weeks**		
FPZ-DEC **(mg)**	Oral FPZ HCI **(mg)**	CPZ-EQ **(mg)**	FPZ-DEC **(mg)**	Oral FPZ HCI **(mg)**	CPZ-EQ **(mg)**	FPZ-DEC **(mg)**	Oral FPZ HCI **(mg)**	CPZ-EQ **(mg)**	FPZ-DEC **(mg)**	Oral FPZ HCI **(mg)**	CPZ-EQ **(mg)**
6.25 (.25 cc)	10	500	6.25 (.25 cc)	5	250	6.25 (.25 cc)	3.3	165	6.25 (.25 cc)	2.5	125
12.5 (.50 cc)	20	1000	12.5 (.50 cc)	10	500	12.5 (.50 cc)	6.6	333	12.5 (.50 cc)	5.0	250
18.75 (.75 cc)	30	1500	18.75 (.75 cc)	15	750	18.75 (.75 cc)	10.0	500	18.75 (.75 cc)	7.5	375
25 (1.0 cc)	40	2000	25 (1.0 cc)	20	1000	25 (1.0 cc)	13.3	665	25 (1.0 cc)	10.0	500
37.5 (1.50 cc)	60	3000	3.75 (1.5 cc)	30	1500	3.75 (1.50 cc)	20.0	1000	3.75 (1.5 cc)	15.0	750
50 (2.0 cc	80	4000	50 (2.0 cc)	40	2000	50 (2.0 cc)	2.63	1315	50 (2.0 cc)	20.0	1000

Note.-Q = quantity. Fluphenazine decanoate (FPZ-DEC) doses are converted to daily oral fluphenazine hydrochloride (oral FPZ HCI) doses and to estimated daily chlorpromazine-equivalent (CPZ-EQ) doses. Decanoate conversions are based on an empirical rule suggested by Kane (25 mg every 3 weeks of decanoate is equivalent to 665 CPZ-EQ per day). These are theoretically determined values and should be interpreted as approximations only. Therefore, comparisons of daily CPZ-EQ doses derived from these values with Patient Outcomes Research Team (PORT)-recommended oral dosing ranges should not be made. However, decanoate doses below the bold line are NOT recommended. Adapted from Zito 1994 and Kane 1996. *Because this formula for conversion from oral to depot dosing is only a very rough approximation, maintenance dosing ultimately should be based on clinical response and side effects. Because 2-3 months are required to achieve steady-state blood levels, oral supplementation should be continued as needed after initiating fluphenazine decanoate and dose adjustments should not be made any more frequently than every 3 months. A loading dose of fluphenazine decanoate can also be used instead of oral supplementation.. (Review reference: Marder et al., 1989).*

Appendix III

Table 3. Chlorpromazine (CPZ) equivalencies and dosing of haloperidol decanoate. See Recommendation 2.

Table 3. Chlorpromazine (CPZ) equivalencies and dosing of haloperidol decanoate

HPL-DEC	Q every month	HPL Q every day	CPZ-EQ
50 mg	(1.0 cc)	5 mg	250 mg
100 mg	(2.0 cc)	10 mg	500 mg
150 mg	(2.5 cc)	15 mg	750 mg
200 mg	(3.0 cc)	20 mg	1000 mg

Note.-Q = quantity. Haloperidol decanoate (HPL-DEC) doses are converted to daily oral haloperidol (HPL) doses and to estimated daily chlorpromazine-equivalent (CPZ-EQ) doses. Decanoate conversions are based on the following rule: 5 mg oral HPL per day is equivalent to 50 mg HPL-DEC every month. These are theoretically determined values and should be interpreted as approximations only. Therefore, comparisons of daily CPZ-EQ doses derived from these values with Patient Outcomes Research Team (PORT)-recommended oral dosing ranges should not be made. Adapted from Zito 1994 and Kane 1996. *Because this formula for conversion from oral to depot dosing is only a very rough approximation, maintenance dosing ultimately should be based on clinical response and side effects. Because 4-6 months are required to achieve steady-state blood levels, oral supplementation should be continued as needed after initiating haloperidol decanoate and dose adjustments should not be made any more frequently than every 4-6 months. A loading dose of haloperidol decanoate can also be used instead of oral supplementation. (Review reference: Marder et al., 1989; Ereshefsky et al., 1993)*

Appendix IV

Algorithm for Maintenance Treatment Considerations: An Example. Recommendations 8-10.

If good initial response

- *Establish lowest effective dose*
- *Minimize side effects*
  - *EPS*
  - *Amenorrhea/sexual side effects*
  - *Weight gain*
  - *Sedation*
  - *Anticholinergic side effects*
- *Optimize quality of life*
  - *Treat negative symptoms*
  - *Social skills training/Social club*
  - *Vocational rehabilitation/Continuing education*
  - *Health status (nutrition, medical care, HIV education, smoking cessation & co-occurring disorders treatment)*

If symptoms persist or relapse despite medication compliance

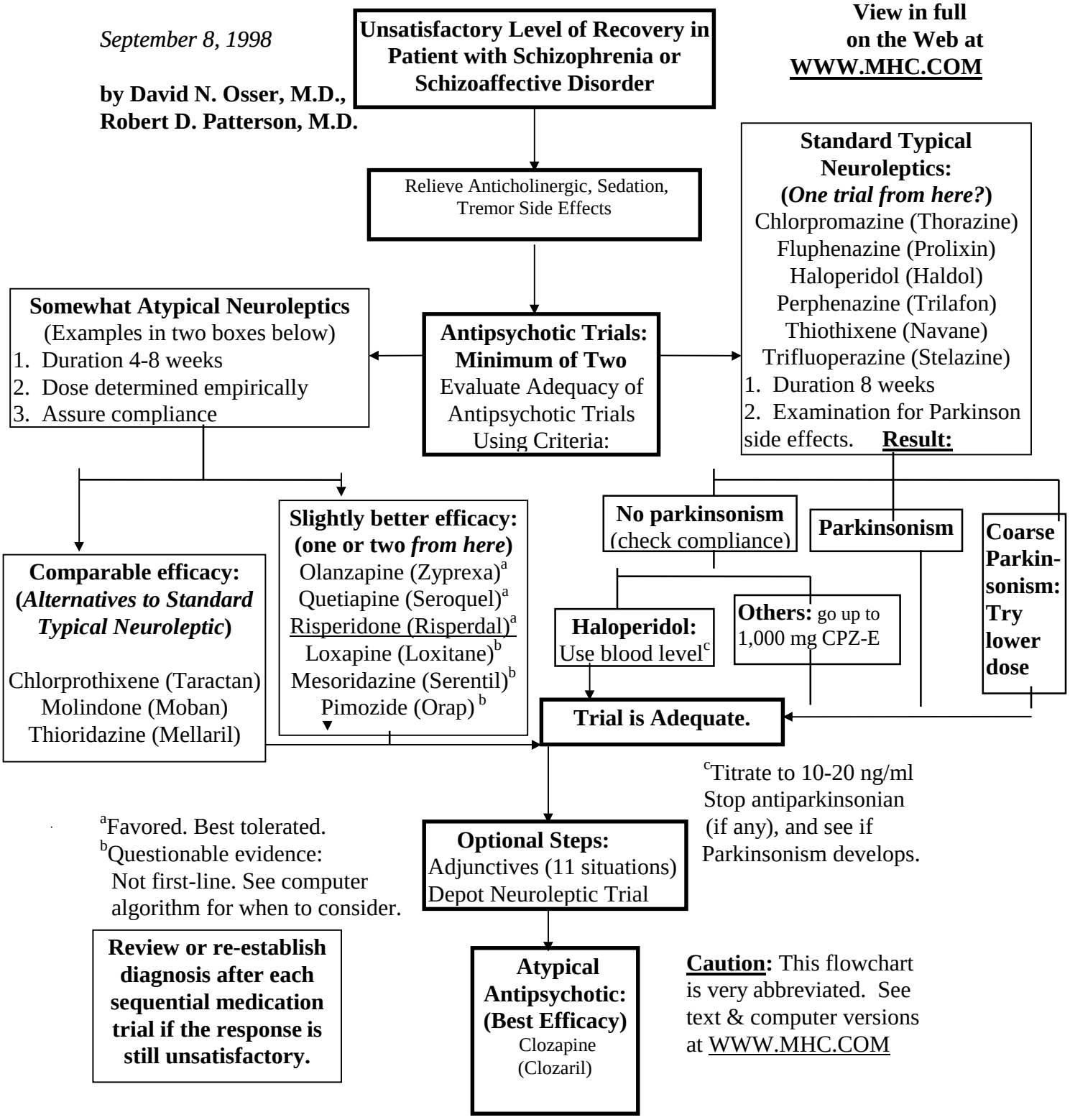
- *Reassess diagnosis*
  - *Substance abuse (offer co-occurring disorders treatment)*
  - *Affective illness (treat accordingly)*
- *Switch to an antipsychotic from a different class*
- *If two adequate trials of two drugs have been performed (including an atypical agent), switch to clozapine*
- *Stress reduction (family meetings, supportive counseling, case management, day treatment)*

If relapse occurs due to noncompliance

- *Psychoeducation*
- *Minimize side effects*
- *Consider depot preparation*
- *Family involvement, supervised residential setting*
- *Outreach/CTT or PACT*
- *Medical guardianship/consider outpatient Rogers'*

Appendix V

Algorithm for Unsatisfactory Response: An Example. (Osser, 1996).



Appendix VI

Levels of Recovery from Psychotic Disorders Chart. See Recommendation 23B.

	ACTIVE ILLNESS (DANGER TO SELF & OTHERS	ACTIVE ILLNESS (CONTROLLED PSYCHOSIS)	STABLE BUT NOT IMPROVING	STABLE & IMPROVING	NORMALIZED ACTIVITY
STAFF SUPERVISION NEEDED	HOSPITAL WARD *locked ward *24 hour nursing care	CUSTODIAL CARE *unlocked ward *day hospital *partial hospital	COMMUNITY RESIDENCE STAFFED *rehabilitation house *3/4, 1/2, 1/4 house	STAFF SUPPORTED APARTMENT *includes other's home	INDEPENDENT LIVING *independent home *flexible support from staff
POSITIVE SYMPTOMS OF ILLNESS	POTENTIAL FOR VIOLENCE *high to moderate risk VOICES *present most of the time, unpleasant THINKING *bizarre, unpleasant REALITY TESTING *poor KNOWLEDGE REGARDING ILLNESS & COMPLIANCE WITH TREATMENT *poor	POTENTIAL FOR VIOLENCE *limited risk VOICES present much of the time, unpleasant THINKING *less bizarre, unpleasant REALITY TESTING *fair KNOWLEDGE REGARDING ILLNESS & COMPLIANCE WITH TREATMENT *poor	POTENTIAL FOR VIOLENCE *minor risk VOICES *present much of the time, unpleasant THINKING *more organized, unpleasant REALITY TESTING *more reality based KNOWLEDGE REGARDING ILLNESS & COMPLIANCE WITH TREATMENT *fair - some denial	POTENTIAL FOR VIOLENCE *minor risk VOICES *less intrusive, viewed as part of illness THINKING *organized, goal-directed REALITY TESTING *reality based most of time KNOWLEDGE REGARDING ILLNESS & COMPLIANCE WITH TREATMENT *fair - less denial	POTENTIAL FOR VIOLENCE *minor or no risk VOICES *none or minimal THINKING *organized, goal-directed REALITY TESTING *good KNOWLEDGE REGARDING ILLNESS & COMPLIANCE WITH TREATMENT *good
NEGATIVE SYMPTOMS OF ILLNESS	FACIAL EXPRESSION *distressed, anxious or flat SPEECH *monotonous voice INTEREST IN OTHERS *avoids close relationships	FACIAL EXPRESSION *distressed, anxious or flat SPEECH *initiates some conversation INTEREST IN OTHERS *does not initiate relationships	FACIAL EXPRESSION *less distressed, anxious SPEECH *better tone, volume INTEREST IN OTHERS *shows interest in others	FACIAL EXPRESSION *demonstrates spontaneous humor SPEECH *give-and-take dialogue INTEREST IN OTHERS *cooperates with others	FACIAL EXPRESSION *adequate range of expression SPEECH *good conversations INTEREST IN OTHERS *enjoys relationships with others
WORK & EDUCATION	VOLUNTEER OR WORK *very limited *concentration for tasks poor *housekeeping room minimal	VOLUNTEER OR WORK *more time with tasks *improved concentration *housekeeping own area	VOLUNTEER OR WORK *day treatment program *psychosocial rehab program *sheltered employment	VOLUNTEER OR WORK *TEP (1/2 time/clubhouse) *supported education *job training	VOLUNTEER OR WORK *independent employment P/T or F/T *independent education *independent volunteer
ADVOCACY	INITIATES SELF ADVOCACY *no self advocacy for needs *no future orientation to goals	INITIATES SELF ADVOCACY *limited self advocacy *limited future orientation to goals	INITIATES SELF ADVOCACY *increasingly voicing own desires *more future goal orientation	INITIATES SELF ADVOCACY *improved sense of self *goals present & future focused	INITIATES SELF ADVOCACY *plans and executes long term goals

Appendix VII

Introduction to the PORT Guidelines (Lehman et al., 1998)

At Issue: Translating Research Into Practice: The Schizophrenia Patient Outcomes Research Team (PORT) Treatment Recommendations

by Anthony F. Lehman, Donald M. Steinwachs, and the Co-Investigators of the PORT Project

The PORT Treatment Recommendations are statements about the treatment of persons with schizophrenia based on substantial scientific evidence. They begin with the assumption that an accurate diagnosis of schizophrenia has been made. They also recognize that treatment for an individual will depend on a variety of factors other than a diagnosis of schizophrenia, such as the presence of other psychiatric and medical conditions, personal and social circumstances, and individual variations. By nature of the fact that the Treatment Recommendations are based on scientific studies, they reflect what is known from well-controlled research. However, this requirement that recommendations be based on substantial scientific evidence means they are silent about or may appear to understate the importance of other aspects of treatment that have not been evaluated adequately. Therefore, there are many more recommendations about pharmacotherapies than about psychosocial treatments. This does not mean that psychosocial treatments are less important than medications, but reflects the fact that we know much less about which psychosocial treatments are helpful. Future research may shed light on these other aspects of care that are often viewed by practitioners, individuals with schizophrenia, and families as vitally important, but for which we lack adequate scientific evidence for efficacy and effectiveness at the present time. Even with these limitations in mind, it is hoped that the PORT Treatment Recommendations will be used to enhance the treatment currently being offered to persons with schizophrenia.

The PORT Treatment Recommendations are organized according to categories of treatments, consistent with the framework of the recently completed review of the treatment literature by the PORT--see ***Schizophrenia Bulletin,*** Vol. 21, No. 4, 1995. The treatment categories are (1) antipsychotic medications; (2) adjunctive pharmacotherapies for anxiety, depression, and aggression/hostility; (3) electroconvulsive therapy; (4) psychological treatments; (5) family treatments; (6) vocational rehabilitation; and (7) assertive community treatment/intensive case management. For each recommendation, a brief rationale and annotations to the above referenced issue of ***Schizophrenia Bulletin*** are provided. These earlier literature reviews offer extensive bibliographies for the interested reader.

The level of evidence for each recommendation is also provided. In writing the recommendations, the PORT investigators adopted the criteria on levels of evidence used for development of the AHCPR Depression Guidelines as follows:

Level A: Good research-based evidence, with some expert opinion, to support the recommendation

Level B: Fair research-based evidence, with substantial expert opinion, to support the recommendations

Level C: Recommendation based primarily on expert opinion, with minimal research-based evidence, but significant clinical experience

We sent initial drafts of these recommendations to experts for review. The experts were asked to rate their level of agreement with each recommendation based on their knowledge of the literature and to provide citations of studies that would argue for revision of the recommendations. Recommendations were modified based on this feedback only if supporting data from published research were provided; that is, opinion alone was not considered adequate to modify a recommendation.

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